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Comparison of Automated and Manual Recording of Brief Episodes of Intracranial Hypertension and Cerebral Hypoperfusion and Their Association with Outcome After Severe Traumatic Brain Injury

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14. ABSTRACT

Adult admissions to a Level I urban trauma center between 2008 and 2010 were reviewed to seek patients with concurrent intraventricular catheter (IVC) and intraparenchymal (IPM) intracranial pressure (ICP) monitor placements. Time periods when ICP data were recorded from both devices were analyzed and compared. While IPM ICP measurements were autonomously recorded at 6-second intervals, IVC ICP values were abstracted from nursing chart recordings. Our study revealed that in this retrospective cohort of 81 adult severe traumatic brain injury patients, IVCs used routinely with only intermittent ICP measurements undervalued ICP when compared to a continuous IPM device. The undervaluing of the IVC compared to the IPM was even more pronounced during periods of elevated ICPs. Our IVC clamping study results, which show that over 30% of the time IVC clamping leads to the elevation of ICP over 20 mmHg, demonstrate the need for a better IVC clamping device design. The newly funded prospective IVC will validate the extent of this challenge and may have great impact in neuro ICP care beyond trauma care.

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1.0 EXECUTIVE SUMMARY

The 2007 Brain Trauma Foundation Guidelines for management of severe traumatic brain injury recommend intracranial pressure (ICP) monitoring utilizing an intraventricular catheter (IVC), also called an extracranial ventricular drain, for salvageable patients with an abnormal head computed tomography scan. IVCs not only provide accurate and reliable ICP measurements, but they also enable therapeutic drainage of cerebrospinal fluid (CSF). Because standard IVCs cannot simultaneously drain CSF and measure ICP, ICP is only routinely measured during brief manual closures of the circuit. We hypothesized that unrecognized, but clinically significant, ICP fluctuations occur during periods of CSF drainage in the care of these patients.

Adult admissions to a Level I urban trauma center between 2008 and 2010 were reviewed to seek patients with concurrent IVC and intraparenchymal (IPM) ICP monitor placements. Time periods when ICP data were recorded from both devices were analyzed and compared. While IPM ICP measurements were autonomously recorded at 6-second intervals, IVC ICP values were abstracted from nursing entries into the patients' vital signs flow sheet and then presumed to remain static until the next IVC ICP measurement was recorded.

Eighty-one patients were identified with concurrent IVC and IPM ICP data over 5579 hours of monitoring. The mean of all the differences between ICP values measured by nurse-recorded IVC vs. auto-recorded continuous IPM showed a difference of -2.42 mmHg (standard error (SE) 0.39 mmHg). Limiting analysis to periods when IPM ICP > 15 and > 20 mmHg, the IVC bias increased to -7.03 (SE 0.38) and -11.02 (SE 0.39) mmHg.

The above finding suggested neurocritical care practice using IVCs for therapeutic CSF drainage with manual ICP measurements undervalues ICP when compared to continuous IPM measurement. This difference is more pronounced in patients with intracranial hypertension and may contribute to additional secondary brain injury and suboptimal functional outcomes.

Our IVC clamping study results, which show that over 30% of the time IVC clamping leads to the elevation of ICP over 20 mmHg, demonstrate the need for a better IVC clamping device design. The newly funded prospective IVC will validate the extent of this challenge and will have great impact in neuro ICP care beyond trauma care.

2.0 INTRODUCTION

Traumatic brain injury (TBI) is a leading cause of death following injury in civilian populations and is a major cause of death and disability in combat casualties [1,2]. Approximately 2 million head injuries occur annually in the United States, resulting in more than 55,000 deaths [3]. Estimates suggest that roughly 20% of all military personnel serving in the current conflicts in the Middle East have suffered some form of TBI, and recent calls for combat casualty care research have specifically targeted advancing TBI care at all echelons of care. The wartime incidence of moderate to severe combat-related TBI (CRTBI) has been reported as 794 penetrating and 652 closed cases, in total 1426 CRTBI cases, between the years 2003 and 2010 [4]. Analysis of U.S. military deaths occurring after arrival at a medical facility found that 9% of potentially survivable and 83% of nonsurvivable "died of wounds" combat deaths were due to CRTBI [5].

The tissue damage that occurs in primary brain injury cannot be treated or regenerated, so management of severe TBI focuses on mitigation of secondary insults. The prevention of

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secondary brain injury focuses on the optimization of cerebral perfusion, and management strategies are aimed at preventing and treating intracranial hypertension (ICH) and cerebral hypoperfusion (CH), both of which are manifestations of elevated intracranial pressure (ICP) and are strongly linked with bad outcomes [6-16]. Cerebral perfusion pressure (CPP) is calculated as mean arterial pressure (MAP) – ICP, and the Brain Trauma Foundation has published recommendations for treatment thresholds for ICP and CPP based on the best currently available evidence [6,17]. Based on these guidelines, our institutional protocol for management of severe TBI aims to maintain ICP below 20 mmHg and CPP above 60 mmHg [6,11,13-15,18].

Currently, two invasive techniques are used for monitoring ICP and CPP. One method requires placement of an intraparenchymal (IPM) fiberoptic pressure monitor that measures and displays ICP continuously. The second method requires placement of an extracranial ventricular drain (EVD). EVD allows therapeutic drainage of cerebrospinal fluid (CSF) as well as measurement of ICP, and it is a preferred choice for severe TBI patients. However, while it is draining, a standard EVD cannot simultaneously measure ICP due to the limitations of the fluid mechanism. ICP measurements are only accurate when the catheter is closed to external fluid drainage. Current neurocritical care practice is to allow continuous therapeutic CSF drainage and to manually close the drain for ICP assessment on an hourly basis. With an EVD, the patient's ICP in the intervening period between the hourly assessments remains unknown. Further, although ICP values are continuously displayed with an IPM pressure monitor, ICP values are still typically only recorded on an hourly basis or when significant prolonged elevations are noted by the clinical staff.

Accurate and clinically useful monitoring of ICP is a key element of these management strategies, and how these data are captured and recorded has significant implications for therapeutic interventions and prognosis. As noted above, the documentation and monitoring of ICP, upon which the assessment of ICH or CH and the need for intervention are based, are most commonly accomplished by manual notation of end-hour recordings of readouts from monitoring systems. This remains the standard of care despite the widespread availability of automated vital signs (VS) recording systems. Recent work from our institution and others has shown that continuous computerized monitoring may have increased sensitivity and specificity in the detection of ICH compared to the manual method [10,19,20]. Continuous recordings of high-resolution, automated electronic VS monitoring data, including ICP and CPP, are more highly correlated with outcomes than manual end-hour recordings [18]. However, current literature in the field of neurotrauma critical care describes ICH and CH as functions of "opening" ICP [10,20-23], maximum or minimum values [16,24], mean values [24-30], number of hourly measurements [9,28,31], or the percentage of time duration regarding different thresholds [31-34], all of which are based on manually recorded data. Our intention in the proposed work is to assess the correlation and quality of data collection from an EVD vs. IPM system to elucidate, quantify, and assess the significance of ICP measurement outside normal range values missed by manual recording procedures and to assess the potential impact on patient outcome of shorter recording intervals than are currently considered standard of care. The work proposed here is grounded on steady increments of analytic and technical monitoring instrumentation achieved at our center and is anticipated to lay the groundwork for the next generation of ICP monitors. It should also provide evidence in support of changing (or retaining) current clinical monitoring protocols.

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3.0 BACKGROUND

3.1 TBI Monitoring

Monitoring the nervous system is critical for trauma patient safety. Continuous real-time monitoring of brain dysfunction could assist clinicians in controlling elevated ICP to avoid secondary brain injury, in rapidly assessing therapy response, and in early adjustment of ICP management plans [35]. The two major monitoring devices for continuous ICP measurement are the IPM ICP monitor and EVDs. Figure 1 illustrates an intraventricular catheter (IVC) used in ICP monitoring. ICP is a complicated function of CSF dynamics, brain tissue resistance, etc. By removing part of fluids or blood clots, ICP may be controlled under a clinically safe level.

Figure 1. Example of an IVC.

Continuously measured ICP is considered useful in improving the prediction of outcomes and hence may help clinicians to better prepare therapeutic plans and improve patients' outcome [36,37]. Many factors may contribute to the selection of one or both devices, such as the need for CSF drainage or clinician preference [38]. Despite the importance of ICP monitoring, some studies showed that there are complications associated with those monitoring methods [39,40]. With 8 years of data from the National Trauma Data Bank, a worsening survival rate was reported to be associated with ICP monitoring for brain-injured patients [41]. The EVD monitoring method has an advantage over the IPM method in that it enables therapeutic drainage of CSF or blood or administration of drugs. However, EVD only allows intermittent IPM-compatible ICP reading when the ventricular drain is closed. For example, in the R Adam Cowley Shock Trauma Center (STC), a regional Level I trauma center, nurses regularly clamp EVDs (i.e., each hour, or every 15 minutes, if ICP is continuously higher than 20 mmHg) and write the reading on charts.

3.2 Clinical Application and Pitfalls

Since EVD monitoring is more and more accepted as standard ICP monitoring [42], more ICP data are measured and recorded from EVDs. It is of practical use to compare the EVD measurement with the IPM one so that interpretations, models, and algorithms based on IPM ICP

could be extended to EVD measurements. Moreover, quantifying the impact of measuring EVD when the ventricular drain is closed could also provide guidance in operating or improving such a device. Three clinical application scenarios have been identified that would benefit from the comparison between the IPM ICP and EVD ICP:

1. Nurse end-hour ICP recording system underestimates automated recording system, with a spread of the difference at the same time.
2. In current automated recording system, 6-second resolution trend data have been widely used. We discovered the optimum recording resolution, which requires less storage, with lower noise level, and helps speed up the data processing time. This provided evidence of the requirement of a new generation of ICP recording systems.
3. EVD drainage could induce an increase in IPM ICP, and we recommended a new mechanism for a drainage system to reduce ICP elevation episodes.

In the comparison of IPM ICP and EVD ICP, there are two potential pitfalls. First, our patient dataset may be limited due to the technical challenges and sporadic nature of continuous monitoring data, which could limit our ability to evaluate the difference between EVD ICP and IPM ICP. Second, due to the complexity of the human brain and our incomplete understanding of TBI physiology, we may have limited ability to describe and interpret the interrelationship of ICP with other VS. In the following study, a comprehensive comparison is made between EVD ICP and IPM ICP to address both potential pitfalls.

3.3   Preliminary Studies

In previous studies, we demonstrated the advantages of automated VS data collection and processing systems compared to manual VS recording in providing data on patients with severe TBI and the power of calculating a pressure-times-time "dose" of ICP and CPP [19,43].Using receiver operating characteristic (ROC) curve techniques, prognostic algorithms were developed correlating VS-related features derived from routine neurotrauma critical care unit electronic monitoring with 30-day mortality and Glasgow Outcome Score-Extended (GOSE) [44] scores at 3 and 6 months. These algorithms were then incorporated into real-time graphic displays of ongoing calculations of Shock Index [Shock Index = systolic blood pressure/heart rate] and Brain Trauma Index (Brain Trauma Index = [CPP/ICP]*time) [45].This prototype patient monitoring video display system is now deployed on a translational basis throughout the STC in Baltimore, MD.

The VS display and feature design in our previous study required IPM ICP. ICP features were designed and their association with outcomes (e.g., mortality, length of hospital stay, GOSE) were evaluated through the ROC and multivariate regression models [36,37]. Using continuous automated ICP measurement, we found that an increase of ICP ≥ 20 mmHg pressure-times-time dose has been associated with higher odds of poor functional outcome [46].With 117 TBI patients, we also studied the drug treatment administrated for ICP control and showed that patients' responsiveness to the treatment may be associated with outcome [47].

In another study [41], we demonstrated that the cumulative number of brief 5-minute episodes of ICH and CH is predictive of poor outcome after severe TBI. This finding has important implications for management paradigms, which are currently targeted to treatment rather than prevention of ICH and CH. This study demonstrates that these brief episodes may

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play a significant role in outcome after severe TBI. The current standard of hourly ICP nursing charting is very likely to miss 5, 10, or 15 minutes of transit ICH and CH. We report the extent of this challenge below.

4.0 METHODS

4.1 Data Sources

4.1.1 Patient Selection. This study were approved by the University of Maryland, School of Medicine Human Research Protections Office and the Air Force Research Laboratory's Institutional Review Board. This is a retrospective study.

From 2008 to 2010, 191 adult TBI patients (age $\geq$ 18 years) with a trauma admission Glasgow Coma Scale (GCS) < 9, a clinically determined requirement for ICP monitoring, and 6-second continuous recorded ICP were available for the study. Patients with severe multi-trauma (more than one non-head Abbreviated Injury Score >3) were excluded. From the total patient cohort, a subset of 81 patients who were monitored simultaneously with both EVD and IPM devices was retrospectively included in the study.

4.1.2 Vital Sings Recording. Continuous IPM (Camino; Integra Lifescience, Plainsboro, NJ) and EVD ICP were recorded every 6 seconds. Nursing-recorded ICP was manually translated into a study database for comparison.

4.1.3 Patient Outcomes. Patient outcomes (recovery assessments, mortality) were evaluated by the clinicians based on patient charts, discharge notes, and patient follow-up visit clinical notes.

4.2 Nurse Charts to Computerized Spreadsheet Table Conversion

Through manual review of nursing charts, hourly Camino IPM ICP, EVD ICP, and MAP were manually translated into the study database (spreadsheet). If quarterly ICPs were recorded, four numbers for 1 hour ICP are also kept in the spreadsheet. Corresponding hourly CPP and MAP were also aligned with ICP records. We organized the nursing data in a spreadsheet with predefined format for efficient parsing and visualization. Figure 2 illustrates this conversion process.
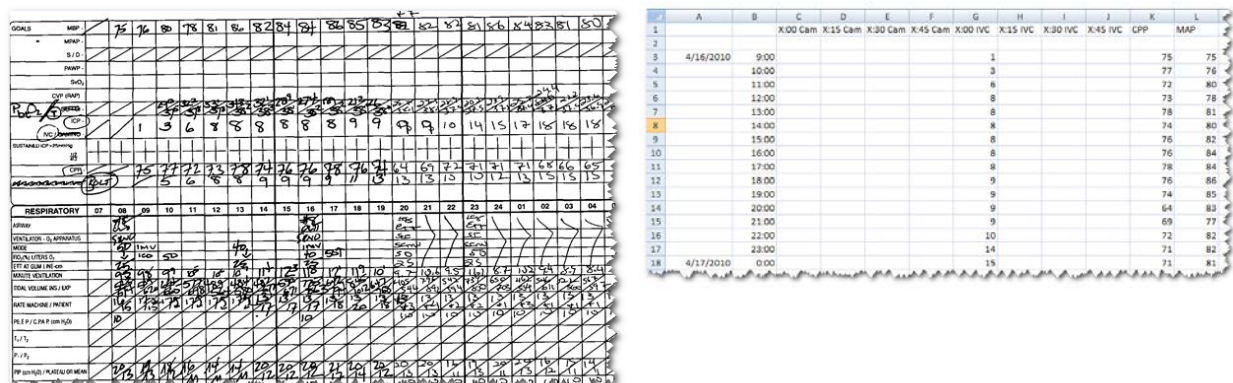
Figure 2. Nurse charts (left) to computerized spreadsheet table (right) for hourly ICP, CPP, and MAP data conversion.

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4.3   Data Verification and Calibration

To validate data from different sources, we visualized all data to verify whether the automated data had temporally aligned with nursing data with no error. For each patient, we plotted the automated ICP data with both 6-second and 5-minute resolution. Over the same time periods, we overlaid the hourly nursing data and verified the time alignment and IPM ICP segments from the automated VS. Figures 3 and 4 show the software that visualizes all the data in a 12-hour time frame. In Figure 3, a segment of Camino automated ICP was flagged by a straight green line. Automated ICPs (6-second and 5-minute resolutions) were plotted in dark green and thin red curves. Hourly nursing ICP data were visualized as a thick red line. Figure 4 shows a segment of automated IVC (auto-IVC) ICP, which was flagged by a straight pink line. The automated 6-second ICP and interpolated 5-minute ICP were also displayed together. Through such visualization and verification, we can segment the data into IPM ICP and IVC ICP for the next step study.
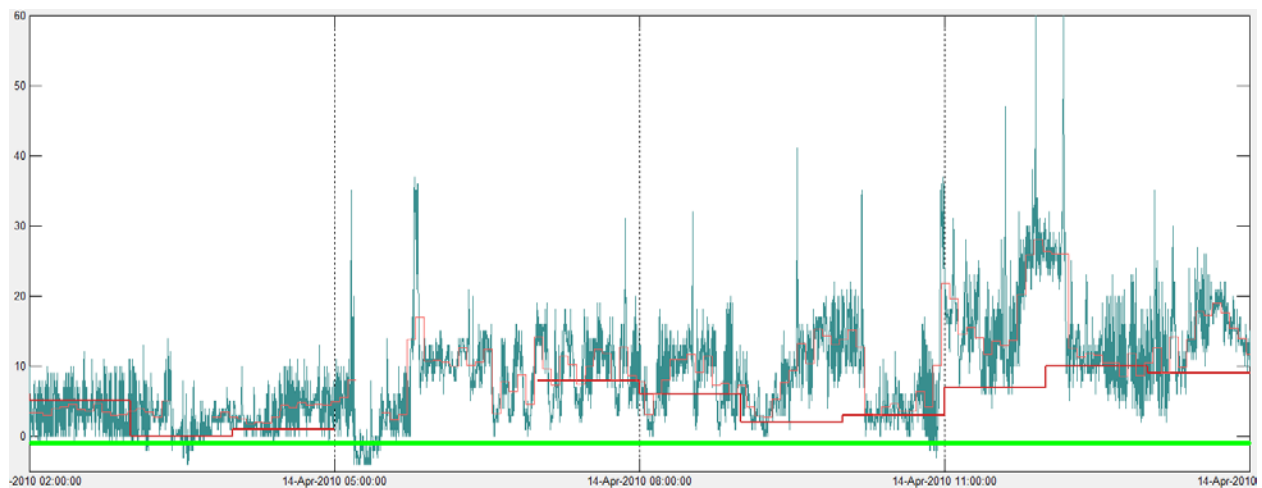
Figure 3. Segment of AutoCam ICP, with nursing ICP data.
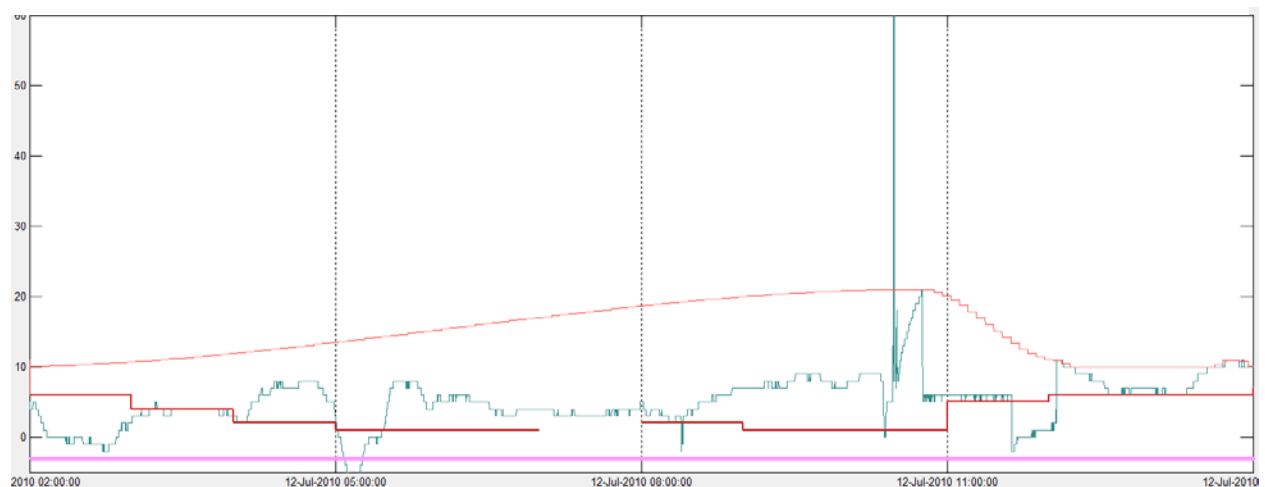
Figure 4. Segment of auto-IVC ICP, with nursing ICP data.

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5.0 RESULTS

5.1 Univariate Prediction Comparison

In this study, we attempted to answer the following two questions:

1. Which individual ICP/CPP features were best predictive of patient outcomes?

2. Does high-resolution auto recording improve prediction compared with nurse recording of ICP values?

Using the segmented data, we compared the discrimination power of two types of ICPs, the automated Camino IPM ICP and the nurse-recorded Camino IPM ICP, in separating the dichotomous outcomes of long-term recovery assessment (>6 months) and near-term recovery assessment (<6 months). We considered a time series of 3 days of automated Camino ICP measurement. We derived 518 features from this segment of time series to summarize its statistical characteristics (e.g., maximum, median, quartiles, etc.) and clinically related quantities (e.g., dose ≥ 20, dose ≥ 30, percentage of time ICP ≥ 20, etc.). To moderate the effect of missing values, we considered the feature value valid only if it was calculated from a time series with more than 50% measurement. With this rule, there were 39 cases included in this study group.

Each single feature derived from 0-1, 1-2, and 2-3 days and accumulative 0-2 and 0-3 days was calculated. With the ROC analysis, we found that a large part of those features had only fair or even no discrimination power of the outcomes, regardless of the ICP type. However, a few features derived from the automated ICP measurement show acceptable discrimination power in the statistical character group features, higher than 0.5 with statistical significance. For example, the first quartile ICP in predicting 3- to 6-month recovery assessment has an area under the ROC (AUROC) of 0.75 ($p = 0.013$). Such features in the nurse-recorded group do not show good discrimination power. Table 1 demonstrates the comparison of ROCs using features derived from the first 24-hour automated ICP and nurse-recorded ICP in predicting the early recovery assessment (<6 months).

Table 1. Comparison of Four Features Derived from Automated ICP and Nurse-Recorded ICP

Feature	Automated ICP		Nurse-Recorded ICP	
	AUROC	p-value	AUROC	p-value
Mean ICP	0.71	0.04	0.64	0.20
Median ICP	0.71	0.05	0.59	0.40
1st quartile ICP	0.75	0.01	0.61	0.32
ICP ≥ 20 mmHg, 5-min episode	0.72	0.04	0.53	0.79

The automated ICP measurement shows some, although limited, stronger discrimination power in separating <6-month recovery assessment outcome than the nurse-recorded measurement. Such difference in outcome prediction performance actually reveals the

disagreement among the ICP monitoring methods. We need in-depth studies to identify where the difference comes from; therefore, we conducted the following studies.

5.2 Quantitative Analysis of Difference in ICP Monitoring Methods

In this study, we attempted to answer the following two questions:

1. During the time both Camino IPM ICP and nurse-recorded IVC EVD ICP were available, how much nurse-recorded EVD ICP underestimated the amount of ICP (mmHg)?
2. When IPM ICP > 20 or > 30 mmHg, how much nurse-recorded EVD ICP further underestimated the amount of ICP (mmHg)?

In comparing ICP monitored by an automated device and nurse recorded, we further distinguished them into IPM ICP (Camino) and EVD ICP (IVC), which are measurements from different monitoring devices. Figure 5 illustrates the possible combinations of measurement data. Measurements were aligned by time and calibrated with respect to temporal resolution. Figure 6 demonstrates the software interface for such data alignment.

	IPM	EVD
Automated	I	III
Nurse-recorded	II	V

Figure 5. Four combinations of measured data from different devices and methods.
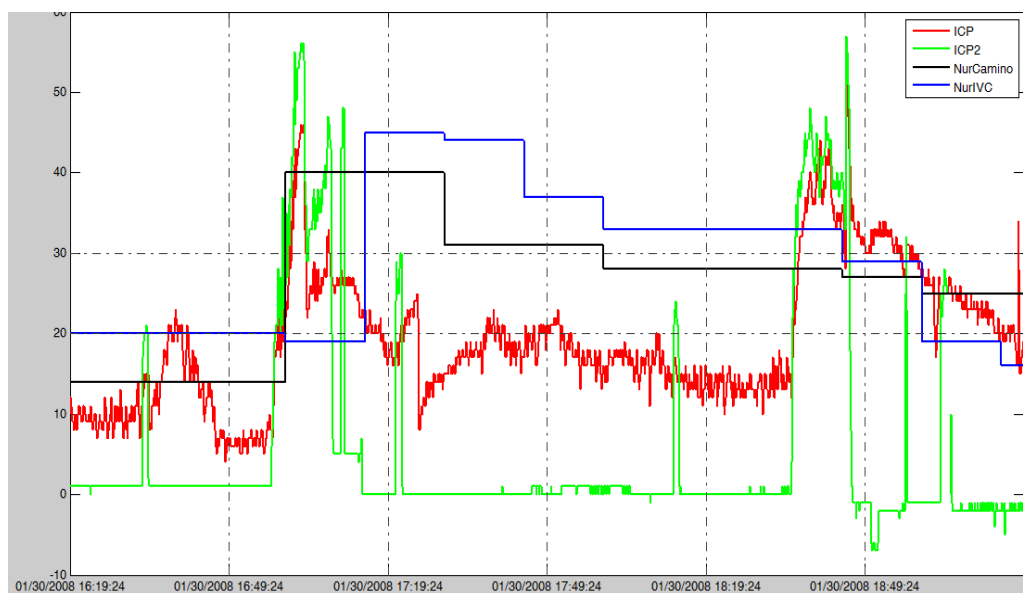
Figure 6. Four measurements aligned by time and calibrated by temporal resolution for comparison.

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The first comparison is based on ICP measurements when both automated Camino (AutoCam) and nurse-recorded IVC (NurIVC) were available. With such criteria, 81 cases among 191 TBI patients were identified. The mortality rate was 19.75%. The average age was 39.8 years old, with first quartile 24.8 years and third quartile 49.3 years. There were 68 males and 13 females in this study group. In terms of the severity, those patients had an average Injury Severity Score of 32.2, with first quartile 25 and third quartile 43. The average admission GCS was 7.42, with first quartile 4 and third quartile 9.25. The average neuro GCS was 7.01, with first quartile 5.5 and third quartile 8.

With all available data in the 81 cases (total measurement 5579 hours), comparisons were conducted at different ICP thresholds with clinical meaning. Besides the overall ICP comparison, we specially examined the measurement difference in the intervals of ICP ≥ 15 mmHg and ICP ≥ 20 mmHg. Table 2 summarizes the difference between AutoCam and NurIVC in terms of mean and standard deviation (SD). In overall comparison, the difference measured by mean and SD shows a small gap between AutoCam and NurIVC. However, as ICP elevates to high intervals, this gap widens, i.e., NurIVC may underestimate the ICP more when ICP increases.

Table 2. AutoCam vs. NurIVC All Records (Mean & SD) (81 Cases)

Statistic	All ICP N=22,315 (5579 h)	ICP ≥ 15 N=5898 (1475 h)	ICP < 15 N=16,487 (4122 h)	ICP ≥ 20 N=1950 (488 h)	ICP < 20 N=20,365 (5092 h)
Mean	-2.06	-6.57	-0.47	-11.07	-1.20
SD	± 6.02	± 7.79	± 4.37	± 9.63	± 4.86

In light of the fact that NurIVC may have different time resolutions, we compared them with AutoCam separately. Based on STC protocol, when ICP is higher than 20 mmHg, NurIVC may happen every 15 minutes instead of every 1 hour. We are interested in whether there are differences between measures taken at these two intervals. Table 3 shows the comparison of AutoCam and NurIVC taken at 15-minute intervals. Table 4 shows the comparison of AutoCam and NurIVC taken at 1-hour intervals. We can see that the gap between the automated measurement and the nurse-recorded one shrinks when the observation frequency is high (15 minutes).

In Figure 7, we summarize the above comparisons in terms of mean, SD, and 95% confidence interval. We can clearly see the pattern that there could be more differences (NurIVC underestimates the ICP) when ICP is high but measured with 1-hour temporal resolution. Such differences may be reduced when NurIVC is taken at 15-minute intervals.

Table 3. AutoCam vs. NurIVC 15-Minute Recording (Mean & SD) (42 Cases)

Statistic	All ICP N=623 (156 h)	ICP ≥ 15 N=403 (101 h)	ICP < 15 N=220 (55 h)	ICP ≥ 20 N=180 (45 h)	ICP < 20 N=443 (111 h)
Mean	1.52	-0.41	5.05	-2.52	3.16
SD	± 7.21	± 6.62	± 7.10	± 6.66	± 6.93

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Table 4. AutoCam vs. NurIVC 1-Hour Recording (Mean & SD) (81 Cases)

Statistic	All ICP N=21,696 (5,424 h)	ICP ≥ 15 N=5377 (1,344 h)	ICP < 15 N=16,319 (4,078 h)	ICP ≥ 20 N=1739 (435 h)	ICP < 20 N=19,957 (4,990 h)
Mean	-2.19	-7.07	-0.58	-12.03	-1.33
SD	± 5.90	± 7.65	± 4.20	± 9.48	± 4.70
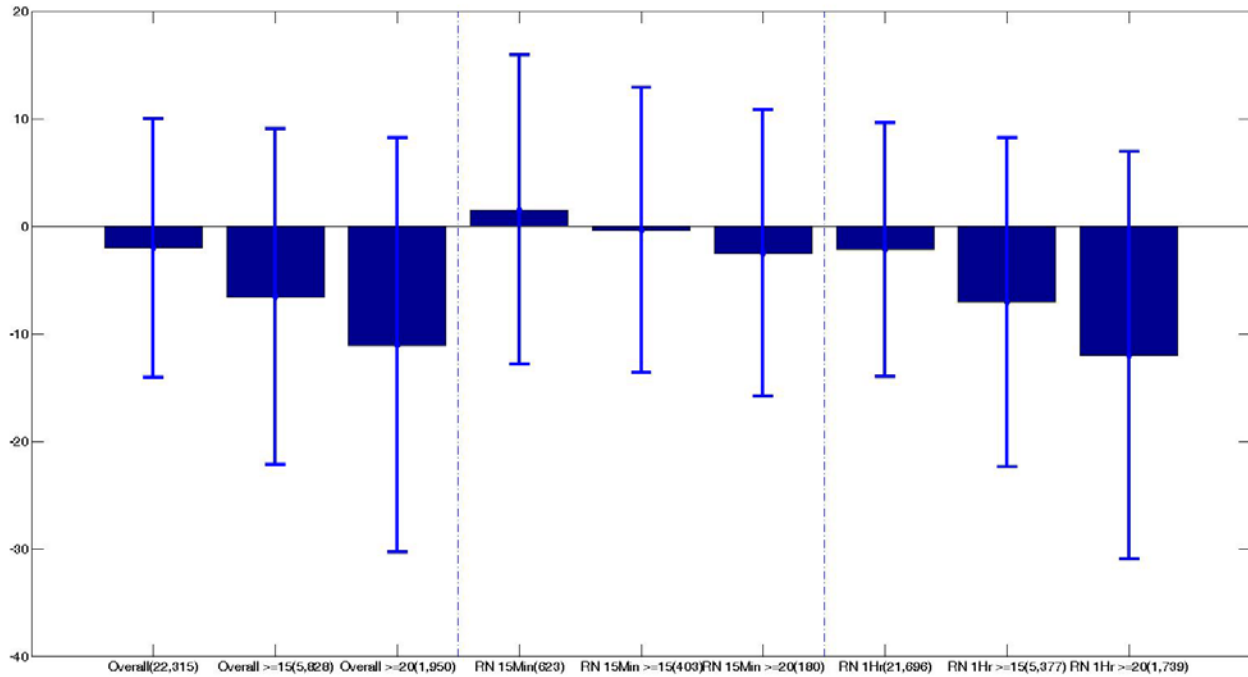
Figure 7. Summary of mean, SD, and 95% confidence interval comparison of three groups of experiments (left: all ICP measurements [all, ≥15 mmHg, ≥20 mmHg]; middle: when NurIVC is at 15-minute intervals only; right: when NurIVC is at 1-hour intervals only).

The bias may be mainly from two sources: the disagreement between NurIVC and AutoCam and the discrepancy between the two ICP measuring devices, the Camino and IVC. To fairly view the difference contributed by the nurse-recorded Camino, we further conducted the second comparison, which compares the AutoCam and nurse-recorded Camino within the 81 cases from the first comparison. There were 28 cases identified (total 374 hours monitoring) within the 81 cases in the first comparison. Table 5 summarizes the gaps at different ICP intervals. In the two Camino measurement types, the gap between automated and nurse recorded is less than between Camino and IVC. Even in the high ICP intervals (ICP ≥ 15 mmHg and ICP ≥ 20 mmHg), the differences are within a small range (-2.60 mmHg ± 5.10 mmHg).

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Table 5. AutoCam vs. NurIVC All Records (Mean & SD) (28 Cases)

Statistic	All ICP N=1495 (374 h)	ICP ≥ 15 N=836 (209 h)	ICP < 15 N=659 (165 h)	ICP ≥ 20 N=360 (90)	ICP < 20 N=1135 (284 h)
Mean	-0.25	-1.51	1.33	-2.60	0.49
SD	± 4.58	± 4.45	± 4.25	± 5.10	± 4.13

The third comparison is based on measurements when both AutoCam and nurse-recorded Camino were available in 191 cases. Such comparison is to extend the study group for more available measurements by relaxing the restriction of comparing within the 81-case group. In total, 80 cases (total 4288 hours measurement) were found satisfying the selection criteria. Table 6 shows the differences in clinically meaningful intervals. From this group, we still observe that NurIVC may underestimate more as ICP elevates if we don't distinguish the manual recording time resolution.

Table 6. AutoCam vs. NurIVC All Records (Mean & SD) (80 Cases)

Statistic	All ICP N=17,152 (4288 h)	ICP ≥ 15 N=5351 (1338 h)	ICP < 15 N=11,801 (2950 h)	ICP ≥ 20 N=1750 (438 h)	ICP < 20 N=15,402 (3851 h)
Mean	-1.17	-3.94	0.08	-7.35	-0.46
SD	± 5.61	± 7.28	± 4.09	± 9.64	± 4.44

5.3   Use Mixed Model to Analyze ICP Data

In the previous sections, we quantitatively analyzed the difference between ICP monitoring methods by comparing the sample means and SDs between them. Such comparison is based on the assumption that observations are drawn from the same population and are independent and identically distributed. Given the multi-level and hierarchical structure of the sequential measurement of ICP among patients, it is not difficult to see that samples between patients are more likely to be independent, while samples from the same patients are more correlated. Hence, there are two sources of variance, within patients and among patients. To model such multiple sources of variation, and to achieve less biased estimation of the difference, we apply the mixed model to analyze the repeated measurement, i.e., the ICP records.

In a mixed model, we consider both the fixed effects and random effects. With each pair of AutoCam and NurIVC, we calculated their difference and used it as the dependent variable. For each patient, we assigned one unique case identification, which was used for grouping variable values according to each patient. As such, the entire 81 patients represent the overall population, and each patient stands for a subpopulation. This approach can take between-patient variation, caused by different nurse, different time, or different recording system, etc., into consideration, and hence provides a less biased estimation.

With all available data in the 81 cases (total measurement 5579 hours), comparisons were conducted at different ICP thresholds with clinical meaning. Beside the overall ICP comparison, we specially examined the measurement difference in the intervals of ICP > 15 mmHg and

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ICP > 20 mmHg. Table 7 summarizes the difference between AutoCam and NurIVC in terms of mean and standard error (SE). In overall comparison, the difference measured by mean and SE shows a small gap between AutoCam and NurIVC. However, as ICP elevates to high intervals, the gap widens, i.e., NurIVC underestimates the ICP more when ICP increases.

Table 7. AutoCam vs. NurIVC All Records (Mean & SE) (81 Cases)

Statistic	All ICP (p<0.05) N^a=22,315 (5579 h)	ICP > 15 (p<0.05) N=5804 (1451 h)	ICP ≤ 15 (p=0.15) N=16,511 (4127 h)	ICP > 20 (p<0.05) N=1947 (487 h)	ICP ≤ 20 (p<0.05) N=20,368 (5093 h)
Mean	-2.42	-7.03	-0.54	-11.02	-1.28
SE	± 0.39	± 0.38	± 0.38	± 0.39	± 0.38

^aN = number of ICP average values in 15-min intervals.

Considering that nurse recordings have different time resolutions (15 minutes or 1 hour), we compared the nurse recordings of each time resolution with AutoCam separately. Based on STC protocol, when a bedside nurse recognizes ICP higher than 20 mmHg, he or she will measure and record the ICP in the patient chart every 15 minutes instead of every 1 hour. We are interested in whether there is a difference between measures taken in these two situations. Table 8 shows the comparison of AutoCam and nurse recordings taken in 15-minute intervals. Table 9 shows the comparison of AutoCam and nurse recordings taken in 1-hour intervals. We can observe that the gap between automated measurement and nurse recordings narrows when the observation frequency is high (15 minutes).

Table 8. AutoCam vs. NurIVC 15-Minute Recording (36 Cases)

Statistic	All ICP (p=0.11) N^a=623 (156 h)	ICP > 15 (p=0.53) N=402 (101 h)	ICP ≤ 15 (p<0.05) N=221 (55 h)	ICP > 20 (p<0.05) N=180 (45 h)	ICP ≤ 20 (p<0.05) N=443 (111 h)
Mean	1.36	-0.52	5.08	-3.27	3.49
SE	± 0.83	± 0.83	± 0.89	± 0.87	± 0.78

^aN = number of ICP average values in 15-min intervals.

Table 9. AutoCam vs. NurIVC 1-Hour Recording (81 Cases)

Statistic	All ICP (p<0.05) N^a=21,528 (5382 h)	ICP > 15 (p<0.05) N=5,320 (1330 h)	ICP ≤ 15 (p=0.12) N=16,208 (4052 h)	ICP > 20 (p<0.05) N=1735 (434 h)	ICP ≤ 20 (p<0.05) N=19,793 (4991 h)
Mean	-2.51	-7.37	-0.59	-11.53	-1.36
SE	± 0.39	± 0.37	± 0.37	± 0.38	± 0.37

^aN = number of ICP average values in 15-min intervals.

5.4 Assess Power of Various Recording Intervals for ICP/CPP to Identify Critical Intervention Opportunities

Almost all the current electronic medical record (EMR) systems will autofill the EMR with instantaneous VS values at the predefined interval such as every 15, 30, or 60 minutes.

This study will highlight the *difference between the instantaneous ICP values vs. average ICP values in 1-, 5-, 10-, 15-, 20-, 30-, 45-, and 60-minute resolutions. Study results could be used to support the selection of VS resolution in the EMR.*

A typical ICP record system often has the following time resolutions: 1-hour resolution data (Q1Hour) in a nurse-based system and 15-minute resolution data (Q15Min) in an electronic-based recording system. In our retrospective dataset, we have 6-second resolution data. These high temporal resolution data allow us to compare and search for a measuring frequency that is a balance between accuracy and cost. In the experiments, we designed two schemes: one is an instantaneous sample at a certain frequency, and the other is a calculation of the average values to represent all measurements in a block of time. Then we set the two schemes in different frequencies, including 1, 5, 10, 15, 20, 30, 45, and 60 minutes. Besides using all measurement data, we further compared the difference when the average ICP (aveICP) is greater than 20 mmHg. Figure 8 illustrates the schemes of using coarse temporal resolution data as ICP measurements. Table 10 summarizes the comparison between instantaneous ICP (inICP) and aveICP at each sampling interval.
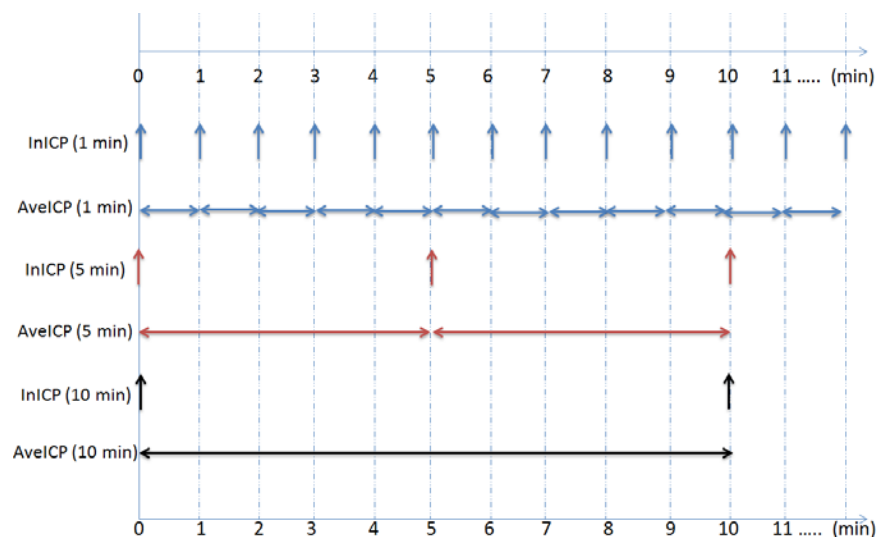
Figure 8. Illustration of various temporal resampling or aggregation schemes.

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Table 10. Comparison Between inICP and aveICP at Different Time Intervals

inICP vs. aveICP Interval (min)	Mean of the Difference Between inICP and aveICP	SD of the Difference Between inICP and aveICP	When aveICP ≥ 20 mmHg, Mean of the Difference	When aveICP ≥ 20 mmHg, SD of the Difference
1	0.09	2.97	-0.37	5.88
5	0.10	3.47	-0.70	6.84
10	0.09	3.88	-1.00	7.31
15	0.10	4.26	-1.13	8.18
20	0.10	4.27	-1.32	7.74
30	0.06	4.41	-1.46	7.02
45	0.11	4.77	-0.98	7.52
60	0.11	5.31	-1.42	11.01

One hundred forty-five TBI patients with 12,611 hours of ICP values were studied. Differences between inICP and aveICP during 5, 15, 30, and 60 minutes were (mean ± SD) 0.10 ± 3.5, 0.10 ± 4.3, 0.06 ± 4.4, and 0.11 ± 5.3 mmHg, respectively (see Table 10). During ICP hypertension (aveICP ≥ 20 mmHg), mean ± SD values between inICP and aveICP at 5, 15, 30, and 60 minutes were -0.70 ± 6.8, -1.13 ± 8.2, -1.46 ± 7.0, and -1.42 ±11.01 mmHg, respectively. All SDs at 15, 30, and 60 minutes were significantly larger than at 5 minutes.

The above results show that the longer the time interval over which inICP was averaged, the larger the variance from the 5-minute data. Especially during ICP hypertension, variances almost doubled in each longer time interval, demonstrating that inICP does not capture interval ICP hypertension. Capture of all ICP hypertension increases fidelity of the electronic record and may improve TBI outcome prediction.

5.5   Mixture Model Analysis to Find the Optimum Resolution

As stated earlier, we used the same mixture model approach to find the optimum ICP resolution from a different point of view. Under such circumstances, the entire 140 patients represent the overall population, and each patient stands for a subpopulation. This approach can take between-patient variation into consideration, which is caused by different nurse, different time, or different recording system, etc., and hence provides less biased estimation. Table 11 summarizes the mixture model analysis results.

5.6   Study of the Association Between EVD ICP Measurement and Elevated ICP Episode

This study was not in the original proposed study list. During our plotting of over 100 ICP comparison cases, we observed that in many instance at the IVC EVD clamp time, Camino IPM ICP rose above 20 or 30 mmHg and took more than 15 or 30 minutes to come back to the initial ICP level.

The following study result, **over 30% of the time EVD clamping leads to the elevation of ICP over 20 mmHg,** indicates the extent of the above pronominal. Based on this study finding, we have obtained a **2-year prospective IPM ICP vs. EVD ICP study** to validate this retrospective study finding.

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If this finding has been cross validated, then a better method of EVD clamping is needed form the sensor manufacturer. **This could help all ICP-monitored patients in any neuro intensive care unit beyond trauma care.**

Table 11. Summary of the Study of Finding the Optimum Resolution for ICP Recording

inICP vs. aveICP Interval (min)	Mean of the Diff Between inICP and aveICP	SE of the Diff Between inICP and aveICP	p-value	Mean of the Diff Between inICP and aveICP (aveICP > 15)	SE of the Diff Between inICP and aveICP (aveICP > 15)	p-value (aveICP > 15)	Mean of the Diff Between inICP and aveICP (aveICP > 20)	SE of the Diff Between inICP and aveICP (aveICP > 20)	p-value (aveICP > 20)
1	0.03	0.03	0.28	-0.20	0.01	<0.05	-0.51	0.02	<0.05
5	0.01	0.04	0.87	-0.28	0.02	<0.05	-0.81	0.03	<0.05
10	-0.01	0.05	0.84	-0.40	0.03	<0.05	-1.06	0.05	<0.05
15	0.00	0.06	0.98	-0.44	0.04	<0.05	-1.16	0.07	<0.05
20	-0.01	0.08	0.87	-0.53	0.05	<0.05	-1.33	0.08	<0.05
30	-0.03	0.09	0.74	-0.64	0.06	<0.05	-1.44	0.11	<0.05
45	0.04	0.12	0.73	-0.47	0.07	<0.05	-0.94	0.15	<0.05
60	0.05	0.15	0.75	-0.70	0.10	<0.05	-1.40	0.19	<0.05

5.6.1 Preliminary Study of Association Between EVD ICP Measurement and Elevated ICP Episode. We observed a pattern frequently appearing in visualized ICP measurements: elevated Camino ICP episodes are accompanied by EVD ICP (IVC) measurements. It is an interesting question to ask if the mechanism of IVC measurement could possibly cause part of the elevation of ICP. We categorized the pattern into five types: (1) elevation of Camino ICP led by IVC measurement with a large dose of ICP ≥ 20 mmHg (see Figure 9); (2) similar to the first one but with a small dose of ICP ≥ 20 mmHg (see Figure 10); (3) elevation of Camino ICP simultaneously with or followed by IVC measurements with a large dose of ICP ≥ 20 mmHg (see Figure 11); (4) similar to the third one but with a small dose of ICP ≥ 20 mmHg; and (4) IVC measurement with no simultaneous and significant change of Camino ICP (see Figure 12). We developed a software interface to mark those event types with time stamps, which could allow us to do the quantitative study in the next stage, such as the duration of elevated ICP, the dose, and the proportion of each event type.
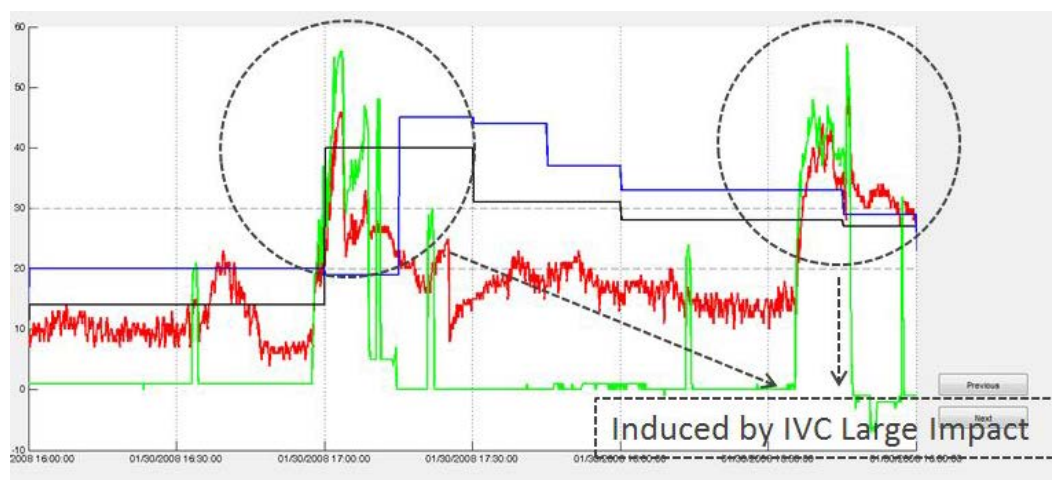
Figure 9. Annotated events for elevated Camino ICP potentially were led by a measurement of IVC, with a large dose of ICP afterward.

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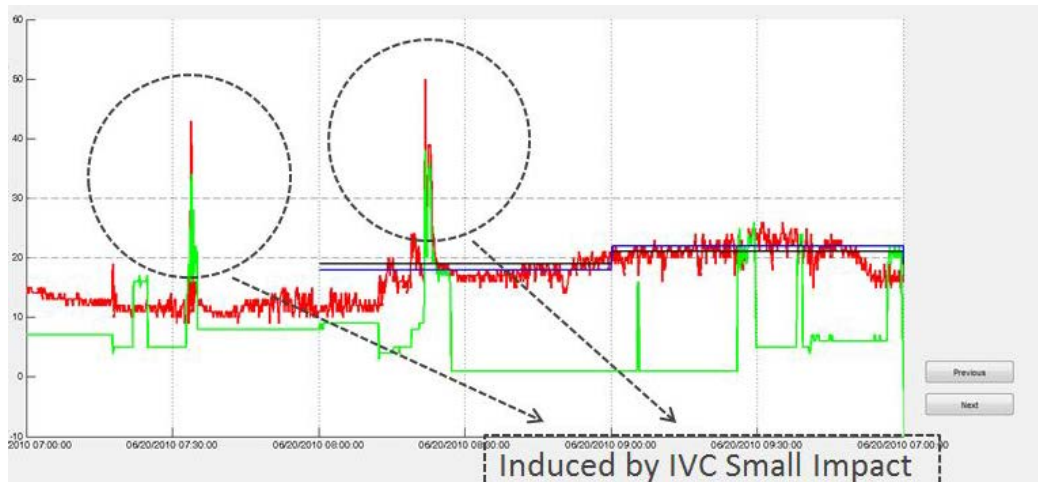
Figure 10. Annotated events for elevated Camino ICP potentially were led by a measurement of IVC, with a small dose of ICP afterward.
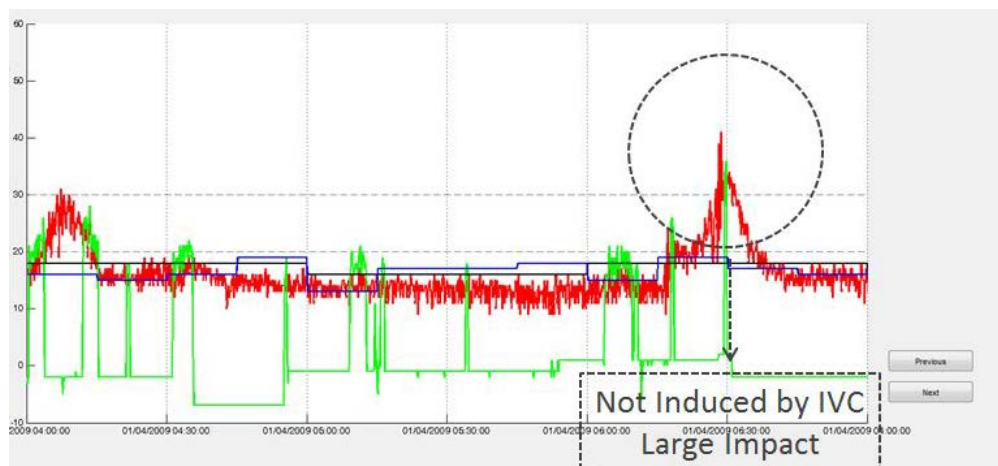
Figure 11. Annotated events for elevated Camino ICP happened simultaneously with a measurement of IVC, with an unignorable ICP dose ≥ 0 mmHg.
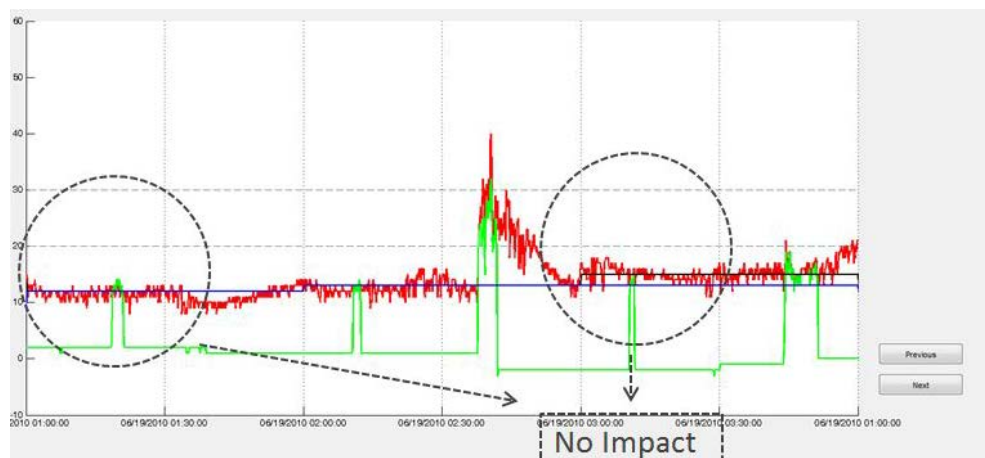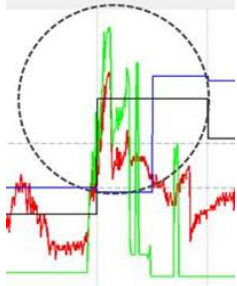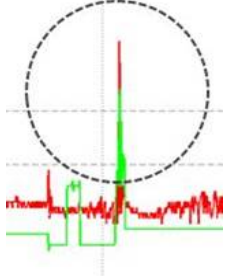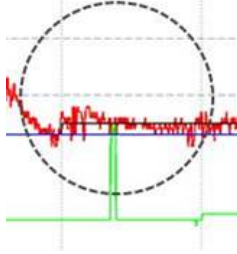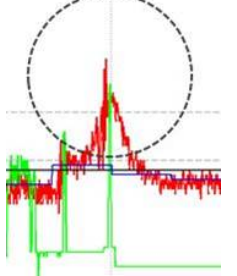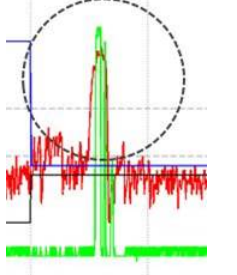
Figure 12. Annotated events for a measurement of IVC without obvious change of AutoCam measurement.

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Table 12 summarizes the description and impact of the five categories.

Table 12. List of Camino and IVC ICP Patterns, Grouped into 5 Categories Based on if the IVC Measurement Induced the Elevation of Camino ICP and Its Impact

Category	Description	Example
IVCL	Large impact of ICP rising above 20 mmHg measured by Camino ICP (red line) likely induced by IVC measurement (green line)	
IVCS	Small impact of ICP rising above 20 mmHg measured by Camino ICP (red line) likely induced by IVC measurement (green line)	
No	No impact between Camino ICP (red line) and IVC measurement (green line)	
L	Large impact of ICP rising above 20 mmHg measured by Camino ICP (red line) not likely induced by IVC measurement (green line)	
S	Small impact of ICP rising above 20 mmHg measured by Camino ICP (red line) not likely induced by IVC measurement (green line)	

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5.6.2 Software for the Study of the Association Between EVD ICP Measurement and Elevated ICP Episode. To extract the detailed feature of the pattern, which is elevated Camino ICP episodes accompanied by EVD ICP (IVC) measurements, such as the time duration, dose, rise slope, drop slope, etc. varying in different patterns, we plotted AutoCam ICP and auto-IVC ICP with 6-second resolution. Over the same time label, we overlaid the hourly nurse-recorded Camino ICP and NurIVC ICP aligned with automated data in a 3-hour time frame. Figures 13 and 14 show the software that visualizes all the data in a 3-hour time frame. The red trace and the green trace represent the AutoCam ICP and auto-IVC ICP in 6-second resolution, respectively, while the black line and the blue line reflect the hourly nurse-recorded Camino ICP and NurIVC ICP correspondingly.
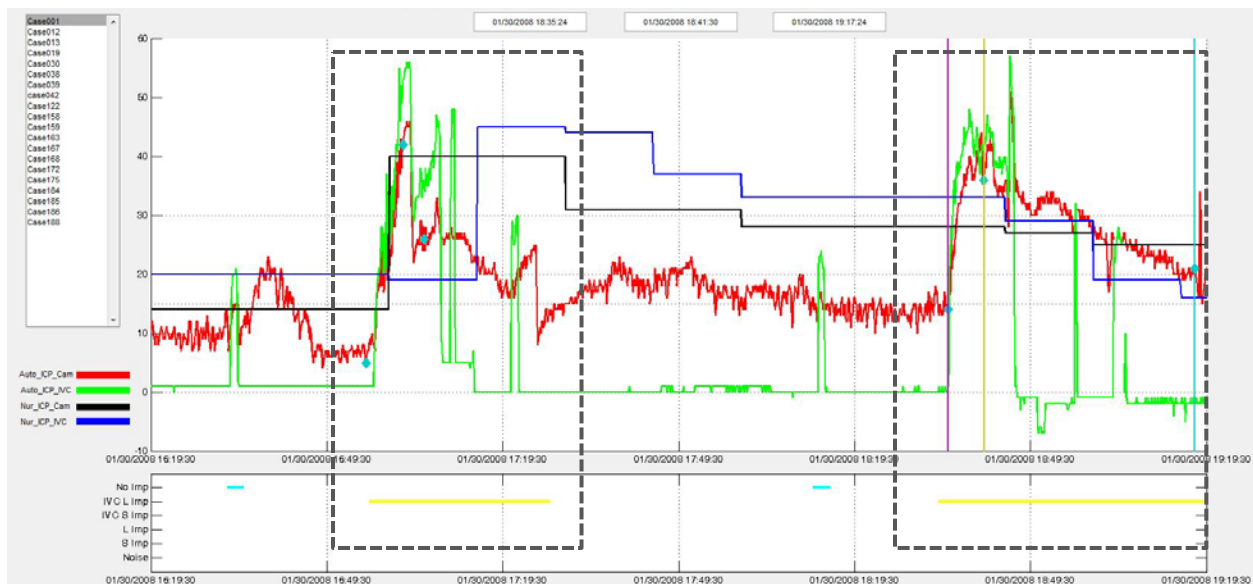
Figure 13. Labeled IVCL episodes.
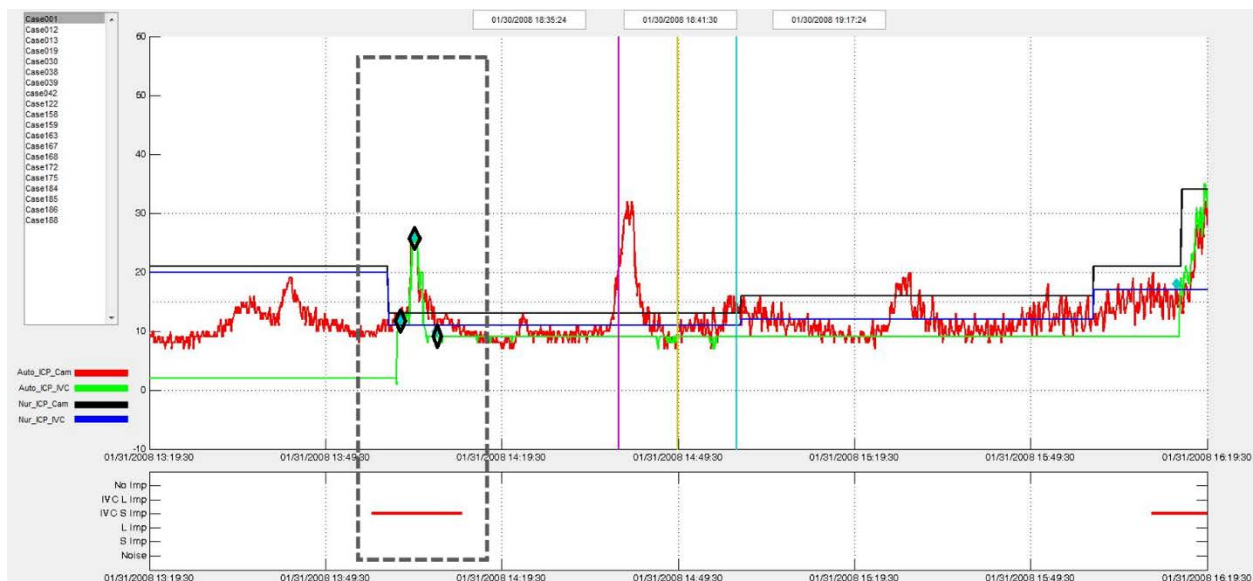
Figure 14. Labeled IVCS episodes.

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In Figure 13, both of the episodes have been labeled as the IVCL category by a yellow straight line. In Figure 14, the highlighted episode has been categorized as IVCS by a red straight line under it. Also, for each of the episodes, we can calculate the rise slope and drop slope indicated by the three diamond-shaped markers.

5.6.3 Feature Extraction in the Study of the Association Between EVD ICP Measurement and Elevated ICP Episode.
Within the master 191 dataset, 18 cases were identified in the current study with AutoCam ICP and auto-IVC ICP recording greater than 12 hours. We first compared the percentage of measurement (number of measurements in each category/total number of measurements).

Figure 15, the stacked bar diagram, shows the statistics for the percentage of the measurements. Each bar in the diagram represents one case. The different colors from bottom to top—blue, red, green, purple, and turquoise—denote the percentage in the category of IVCL, IVCS, L, S, and No, respectively. The table sitting on top of the bar diagram shows the total time duration of both AutoCam ICP and auto-IVC ICP recorded, and the total number of measurements have been identified as well. The table under the bar diagram indicates the patients' demographic data and outcomes: mortality, 0-6 weeks GOSE, 6 weeks – 3 months GOSE, 3-6 months GOSE, and > 6 months GOSE.

	C001	C012	C013	C019	C030	C038	C039	C042	C122	C158	C159	C163	C167	C168	C172	C175	C184	C186
Time Duration (hr)	70.40	107.77	62.76	113.19	95.39	77.66	16.45	118.61	27.93	94.92	26.75	36.61	40.12	22.83	66.64	32.34	143.06	119.53
Measurements (M)	60	55	36	126	79	35	10	115	23	93	12	31	9	29	16	9	47	15

	C001	C012	C013	C019	C030	C038	C039	C042	C122	C158	C159	C163	C167	C168	C172	C175	C184	C186
Age	29	42	26	18	23	19	19	48	18	19	19	30	42	44	41	45	20	39
Gender	F	M	M	M	M	F	M	F	M	M	M	M	M	M	M	M	M	F
Mortality	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
Early	1		1			1	1	1	0	1	1	1		1	1	1		0
Mid	1	0	1	0	0	1	1	1	0	0		1		1	1	1	1	1
Late	1	0	1	0	0	1	0	0	0	0		0		1		1	0	
Long	0	0	1	0	0	1	1	0	0	0		0		1			0	

Figure 15. Percentage of measurements in different categories.

We hypothesized the percentage of the number of measurements in different categories could be an indicator of bad outcomes. Under such circumstances, Case 172 and Case 001, with the first and third highest value of the percentage of IVCL and IVCS, both showed bad GOSEs, while Case 012, with the second highest percentage, lived and had good GOSEs. In this case, using the percentage to predict outcomes is not conclusive yet.

Using the same format and color code as in Figure 15, Figures 16, 17, and 18 display the percentage of time duration in different categories using different thresholds, ICP ≥ 15, ICP ≥ 20, and ICP ≥ 30, respectively.

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	C001	C012	C013	C019	C030	C038	C039	C042	C122	C158	C159	C163	C167	C168	C172	C175	C184	C186
ICP >= 15 (hr)	33.19	21.06	36.96	92.66	50.54	18.81	4.83	53.67	11.53	41.55	1.58	8.60	22.92	13.24	32.80	1.11	111.82	64.95
Perc of ICP >= 15	47.14%	19.54%	58.89%	81.86%	52.98%	24.22%	29.36%	45.25%	41.29%	43.78%	5.89%	23.50%	57.12%	57.98%	49.22%	3.43%	78.16%	54.34%

	C001	C012	C013	C019	C030	C038	C039	C042	C122	C158	C159	C163	C167	C168	C172	C175	C184	C186
Age	29	42	26	18	23	19	19	40	18	19	19	30	42	44	41	45	20	39
Gender	F	M	M	M	M	F	M	F	M	M	M	M	M	M	M	M	M	F
Mortality	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
Early	1		1			1	1	1	0	1	1	1		1	1	1		1
Mid	1	0	1	0	0	1	1	1	0	0		1		1	1	1	0	1
Late	1	0	1	0	0	1	0	0	0	0		0		1		1	0	1
Long	0	0	1	0	0	1	1	0	0	0		0		1			0	

Figure 16. Percentage of time duration in each category as ICP ≥ 15.

In Figure 16, the table on top of the bar diagram indicates the time duration ICP ≥ 15 and the percentage of time that ICP ≥ 15. The table under the diagram gives us some of the patients' demographic data and the outcomes. As the information shows in Figure 16, Case 159, which experienced only 1.58 hours of ICP ≥ 15, only 5.89% of the time, has the lowest percentage of measurement time of IVCS. Also, Case 175, which was measured within 3.43% of 1.11 hours, has a percentage of measurement time of IVCS almost as low as that of Case 159.

	C001	C012	C013	C019	C030	C038	C039	C042	C122	C158	C159	C163	C167	C168	C172	C175	C184	C186
ICP >= 20 (hr)	16.70	12.64	11.77	48.70	16.09	3.29	2.42	15.10	1.33	16.07	0.32	2.34	10.00	1.28	0.90	0.52	53.49	36.61
Perc of ICP >= 20	23.72%	11.73%	18.75%	43.02%	16.87%	4.24%	14.72%	12.73%	4.76%	16.93%	1.21%	6.39%	24.93%	5.62%	1.35%	1.59%	37.39%	30.63%

	C001	C012	C013	C019	C030	C038	C039	C042	C122	C158	C159	C163	C167	C168	C172	C175	C184	C186
Age	29	42	26	18	23	19	19	40	18	19	19	30	42	44	41	45	20	39
Gender	F	M	M	M	M	F	M	F	M	M	M	M	M	M	M	M	M	F
Mortality	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
Early	1		1			1	1	1	0	1	1	1		1	1	1		1
Mid	1	0	1	0	0	1	1	1	0	0		1		1	1	1	0	1
Late	1	0	1	0	0	1	0	0	0	0		0		1		1	0	1
Long	0	0	1	0	0	1	1	0	0	0		0		1			0	

Figure 17. Percentage of time duration in each category as ICP ≥ 20.

	C001	C012	C013	C019	C030	C038	C039	C042	C122	C158	C159	C163	C167	C168	C172	C175	C184	C186
ICP >= 30 (hr)	4.34	3.82	0.25	4.27	2.49	0.08	0.24	0.90	0.15	2.88	0.08	0.26	0.70	0.17	0.01	0.27	4.21	4.37
Perc of ICP >= 30	6.16%	3.54%	0.39%	3.77%	2.61%	0.10%	1.46%	0.75%	0.53%	3.04%	0.29%	0.70%	1.74%	0.74%	0.01%	0.83%	2.94%	3.65%

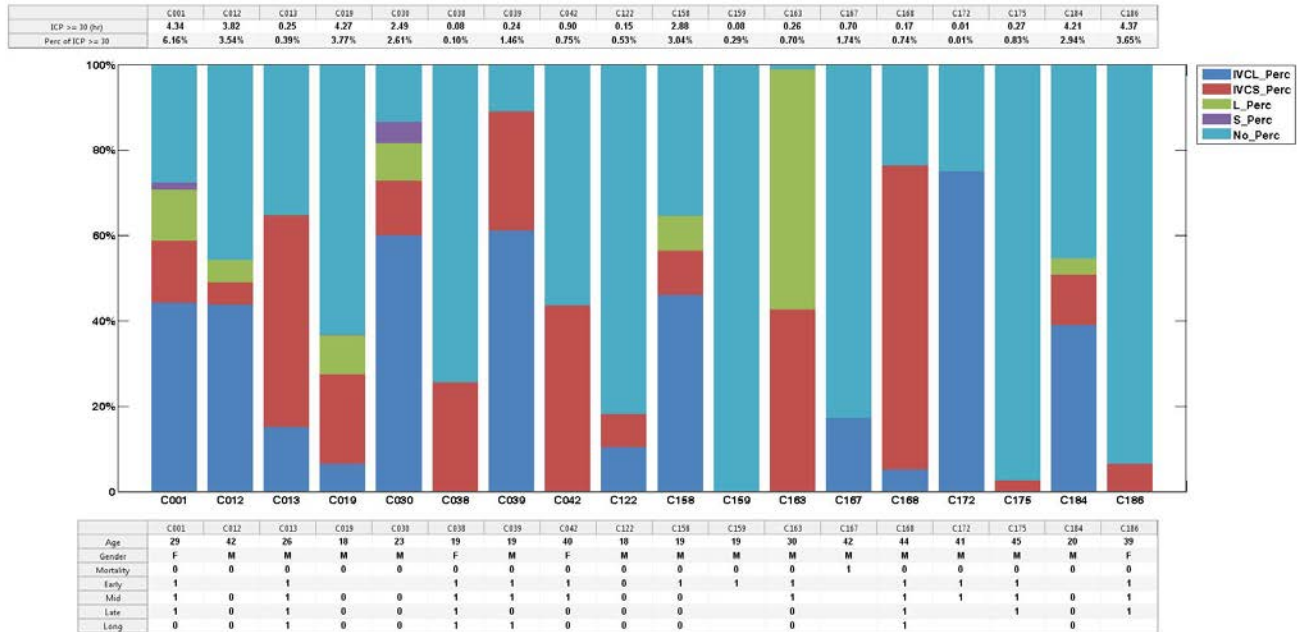|	C001	C012	C013	C019	C030	C038	C039	C042	C122	C158	C159	C163	C167	C168	C172	C175	C184	C186
Age	29	42	26	18	23	19	19	40	18	19	19	30	42	44	41	45	20	39
Gender	F	M	M	M	M	F	M	F	M	M	M	M	M	M	M	M	M	F
Mortality	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
Early	1		1			1	1	1	0	1	1	1		1	1	1		1
Mid	1	0	1	0	0	1	1	1	0	0		1		1	1	1	0	1
Late	1	0	1	0	0	1	0	0	0	0		0		1		1	0	1
Long	0	0	1	0	0	1	1	0	0	0		0		1			0	

Figure 18. Percentage of time duration in each category as ICP ≥ 30.

If we compare the bar diagrams in Figures 16-18, it is easily seen that the height of different color bars increases as the threshold changes from 15 to 30. In other words, the percentage of time duration for different categories increases as ICP elevates from 15 to 30. We observed the same pattern for the feature of dose as threshold increasing from 15 to 30.

Besides the above comparisons, we further compared the different features (i.e., time percentage of ICP > 15, 20, and 30 mmHg, dose of ICP > 15, 20, and 30 mmHg) for the same case. Figures 19 and 20 are two individual cases as examples. The increasing pattern for both features (time duration and dose) could be observed.
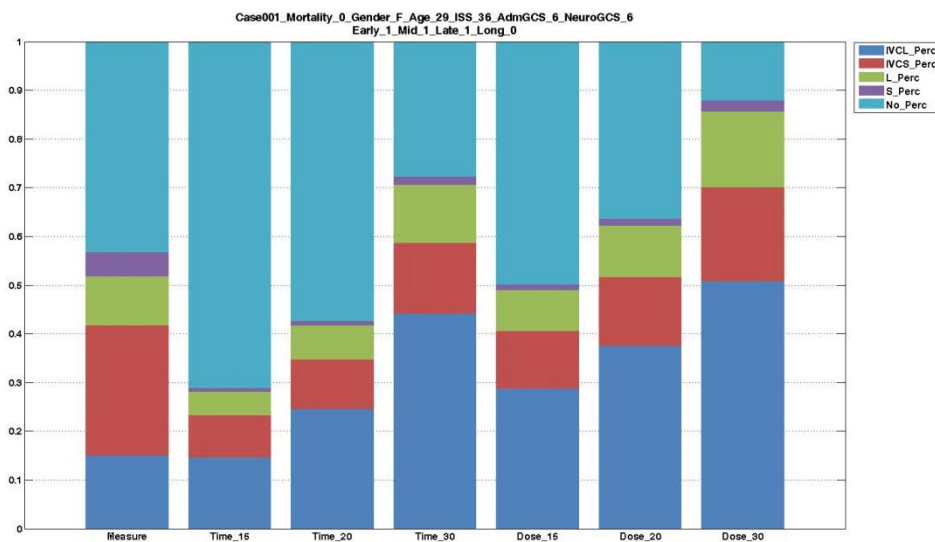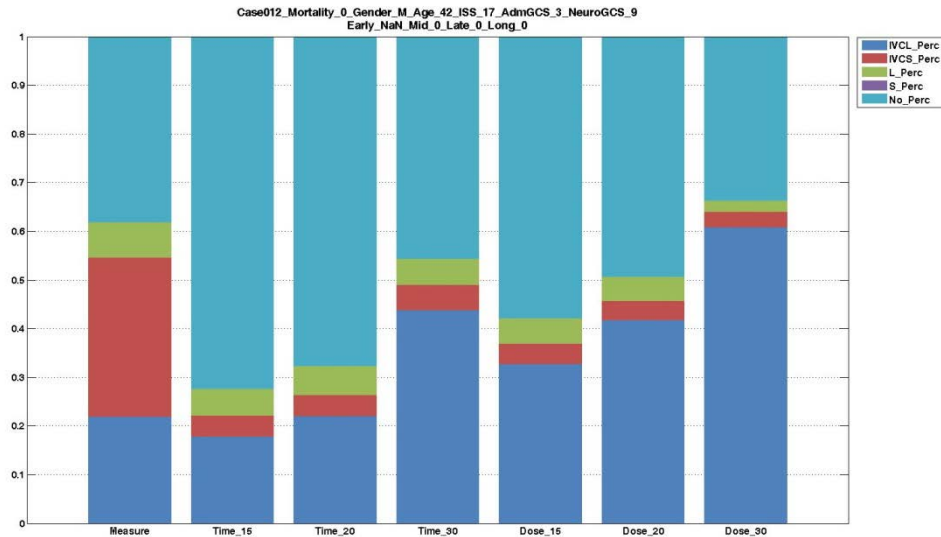

Figure 19. Feature comparison for Case 001.

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Case012_Mortality_0_Gender_M_Age_42_ISS_17_AdmGCS_3_NeuroGCS_9
Early_NaN_Mid_0_Late_0_Long_0

Figure 20. Feature comparison for Case 012.

6.0 DISCUSSION

ICP monitoring is a key element in the ICP- or CPP-oriented management of severe TBI. ICP is used to predict outcome, to alert caregivers of herniation risk, and to guide therapy to primarily maintain CPP. Because ICP cannot be reliably estimated by noninvasive methods or by computed tomography imaging, placement of an invasive device, typically an IVC EVD or Camino IPM, is recommended by the Brain Trauma Foundation (BTF) in most of these patients. In patients at high risk for intracranial hypertension, an IVC is preferred, as it permits therapeutic CSF drainage, although CSF drainage sacrifices the capability to continuously monitor ICP. Therapeutic CSF drainage may be insufficient alone to reduce ICP below the recommended upper threshold of 20-25 mmHg.

In addition to its therapeutic function, an IVC is also expected to be used as a monitoring method for ICP. Currently, the readings are often obtained by nurses clamping the EVD and writing down the reading on nurse charts regularly. The manually recorded IVC ICP sequences have different time resolutions compared with automated, continuous, high temporal resolution IPM measurement. Our study found that intermittent IVC ICP values have lower discriminant power than the continuous (6-second) IPM ICP in predicting long-term outcomes, such as mortality and early recovery assessment (<6 months). Therefore, if treatment is of top priority, IVC-type measurement should be selected. On the other hand, if it is more important to gather precise data for a treatment plan, IPM measurement could be a better choice, or the use of IVC measurement with clamping for a long time.

The difference of prediction power between IVC and IPM ICPs can also be quantified by their statistical characteristics. Our study revealed that in this retrospective cohort of 81 adult severe TBI patients, IVCs used routinely with only intermittent ICP measurements undervalued ICP when compared to a continuous IPM device. The undervaluing of the IVC compared to the IPM was even more pronounced during periods of elevated ICPs. Adherence to the BTF guidelines for ICP and CPP management is associated with improved survival in severe TBI patients [48]. Previous work at our institution suggested that even brief, 5-minute episodes of

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intracranial hypertension and cerebral hypoperfusion cumulatively predict worsened secondary insult and worsened outcome [pressure-time dose, mmHg x h] [43]. Overall, these findings are worrisome that standard neurocritical practices utilizing IVCs may completely miss brief episodes and/or delay management of sustained episodes of intracranial hypertension that contribute to secondary brain injury and suboptimal functional outcomes.

Due to its dual functionality, IVC-type measurement gains more and more acceptance. However, clamping EVD for measuring interrupts the treatment and brings changes to the CSF, which may cause temporal or local changes of ICP. Our IVC clamping study results, **over 30% of the time IVC clamping leads to the elevation of ICP over 20 mmHg,** demonstrate the need for better IVC clamping device design. From case-based studies, patients with unfavorable outcomes have a larger proportion of time of dose with elevated ICP with preceding IVC clamping. The loss or compromised autoregulation could explain the weakened responsiveness to external stimuli and change of CSF after clamping. Since sustained elevation of ICP is associated with higher mortality rate or other unfavorable outcomes, it is necessary to prevent introducing unnecessary high ICP episodes during ICP monitoring. Therefore, more evaluation should be carried out to quantify how patients respond to the IVC-type measurement, especially for patients who may already have lost autoregulation. The newly funded prospective IVC and Camino IPM study will validate the extent of this challenge and may have great impact in neuro ICP care beyond trauma care.

In the 2007 BTF guidelines, further improvement in ICP monitoring technology is cited as a key issue for future investigation. The development of multiparametric ICP devices that can provide simultaneous measurement of ventricular CSF drainage, parenchymal ICP, and other advanced monitoring parameters is advocated. We strongly agree with this critical need since current monitoring practices provide "only part of the story."

7.0 CONCLUSIONS

ICP monitoring is a key component in ICP management. Selection of monitoring devices is a complicated trade-off between reliability, availability, treatment, and clinician preference. Invasive ICP monitoring is so far the "gold standard" compared with noninvasive approaches. Using it or selecting different ICP monitoring methods depends on various factors. As EVD ICP has its advantage in allowing monitoring and therapeutic drainage or drug administration, it is receiving wider acceptance in TBI patient monitoring. The intermittent nurse reading of ICP by clamping EVD provides valuable but underestimated ICP, based on our comparison of ICP measurements with EVD and IPM ICPs simultaneously available. More importantly, clamping EVD may have an impact on TBI patients under ICP monitoring. Therefore, more thorough studies, such as controlled simulation of pressure change during CSF drainage, and even larger study populations could aid the precise identification of EVD measurement complication, as well as the design of an improved EVD device that could minimize the negative effect.

7.1 Immediate Impact

Our study provided noticeable, although preliminary, evidence that the widely used EVD ICP monitoring device may be associated with some unexpected elevation of ICP during its measurement. If this negative effect of clamping EVD measurement can be further confirmed with more study cases, the way of using the EVD device and its design would be changed to

avoid impact on TBI patients with limited or lost responsiveness to external stimuli. For example, in the manual operation of the EVD device, the hole could be closed slowly. An electronic micro-motor could be installed to control the speed of clamping.

This study also suggests that regular monitoring could also have physical influence on TBI patients, and patients' neurological responsiveness could be estimated from ICP changing patterns before and after EVD measurement. Future studies could include EVD measurement responsiveness, which could be used together with drug treatment responsiveness for better evaluating patients' neurologic condition.

7.2   Limitations

This study is limited by its retrospective nature and modest patient sample size. Although continuous data provide us a large amount of data points, we had limited number of patients in this study, especially for those with adverse outcomes. There may be differences in the ICP values intrinsic to the modalities themselves (ventricular vs. parenchymal ICP), their location within the cranial vault, and "measurement drift" in the IPM since it cannot be recalibrated after placement. Additionally, the specific clinical rationale for periods of simultaneous IVC and IPM device placement were not available nor whether management interventions were initiated based upon the IPM ICP value prior to the next recorded IVC ICP value. There are also other factors that may dominate the reason for patient adverse outcomes, such as mechanism of injury, patient history, drug use, etc. Therefore, stronger conclusions could only be drawn when we control those factors.

8.0   REFERENCES

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LIST OF ABBREVIATIONS AND ACRONYMS

AutoCam   automated Camino

Auto-IVC   automated IVC

aveICP   average ICP

BTF   Brain Trauma Foundation

CH   cerebral hypoperfusion

CPP   cerebral perfusion pressure

CRTBI   combat-related traumatic brain injury

CSF   cerebralspinal fluid

EMR   electronic medical record

EVD   extraventricular drain

GCS   Glasgow Coma Scale

GOSE   Glasgow Outcome Score-Extended

ICH   intracranial hypertension

ICP   intracranial pressure

inICP   instantaneous ICP

IPM   intraparenchymal

IVC   intraventricular catheter

IVCL   large impact of ICP rising above 20 mmHg measured by Camino ICP likely induced by IVC measurement

IVCS   small impact of ICP rising above 20 mmHg measured by Camino ICP likely induced by IVC measurement

MAP   mean arterial pressure

NurIVC   nurse-recorded IVC

ROC   receiver operating curves

SD   standard deviation

SE   standard error

SpO$_2$ oxygen saturation

STC   R Adam Cowley Shock Trauma Center

TBI   traumatic brain injury

VS   vital signs